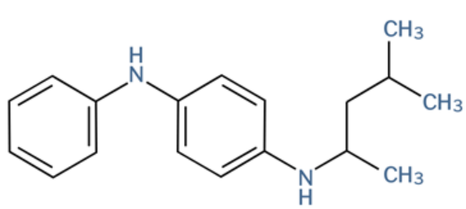
What We Know: 6PPD and 6PPD-quinone

In the short time since 6PPD-quinone (6PPD-q) was isolated and characterized, scientists have been working to understand its prevalence and behaviors in the environment. This focus sheet provides environmental officials with a brief overview of the current understanding of 6PPD-q sources, exposure, fate, transport, toxicity, and mitigation strategies. In-depth ITRC guidance will be released in summer 2024.

In 2020, researchers in Washington State discovered and identified 6PPD-quinone (6PPD-q) as the stormwater chemical responsible for urban runoff mortality syndrome observed in coho salmon (*Oncorhynchus kisutch*) around Puget Sound over the last 25 years.[1,2] Research has demonstrated that 6PPD-q is also acutely lethal to brook trout[3] and rainbow trout/steelhead.[3–5] 6PPD is the primary anti-degradant in tires and has been in use since the 1960s. 6PPD-q is one of the products formed by the reaction of 6PPD and ozone (Figure 1). 6PPD-q may be present in many places impacted by tire use. 6PPD and 6PPD-q have been detected in stormwater and surface waters on many continents[1,6–10] and have been found in airborne particulates,[11–14] sediment,[15] soil,[11] rubber products other than tires,[16] and human urine.[17]

6PPD

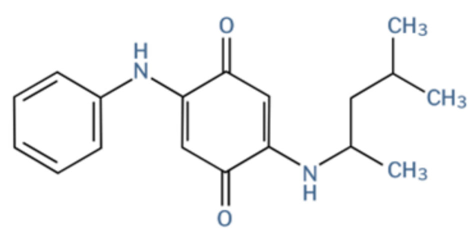
1,4-Benzenediamine, N-(1,3-dimethylbutyl)-N'-phenyl-



CASRN 793-24-8

6PPD-quinone

2-anilino-5-[(4-methylpentan-2-yl)amino] cyclohexa-2,5-diene-1,4-dione



CASRN 2754428-18-5

Figure 1. Chemical structures for 6PPD and 6PPD-quinone.

How Is 6PPD-q Entering Surface Waters?

Tire wear particles (TWPs) containing 6PPD-q are transported via stormwater to surface water (Figure 2). Many urban stormwater systems are designed to control flooding, not capture and treat contaminants. In separate storm sewer systems, rainwater is transported to natural receiving waters through a network of ditches and pipes without natural or engineered green spaces to remove pollutants prior to entering surface waters. Additionally, some areas with installed stormwater best management practices (BMPs) are failing to contain stormwater due to increased urbanization and storm events that are larger than the infrastructure was designed for, leading to direct conveyance of 6PPD-q to vulnerable aquatic ecosystems.

What We Know: 6PPD and 6PPD-quinone

Multiple aspects of the lifecycle of 6PPD-q are under investigation. This includes the factors that influence the formation of 6PPD-q in tires and tire wear particles (TWPs) in the environment, 6PPD-q's leaching rates from TWPs, and its persistence and bioaccumulation potential. Programs that divert scrap tires from landfills recycle the tires into crumb rubber materials used on sports fields, rubber-modified asphalt, tire-derived aggregate used in civil engineering projects, and more. The levels of 6PPD-q released from recycled tire products is also actively being researched.

Conceptual Transport and Exposure Model

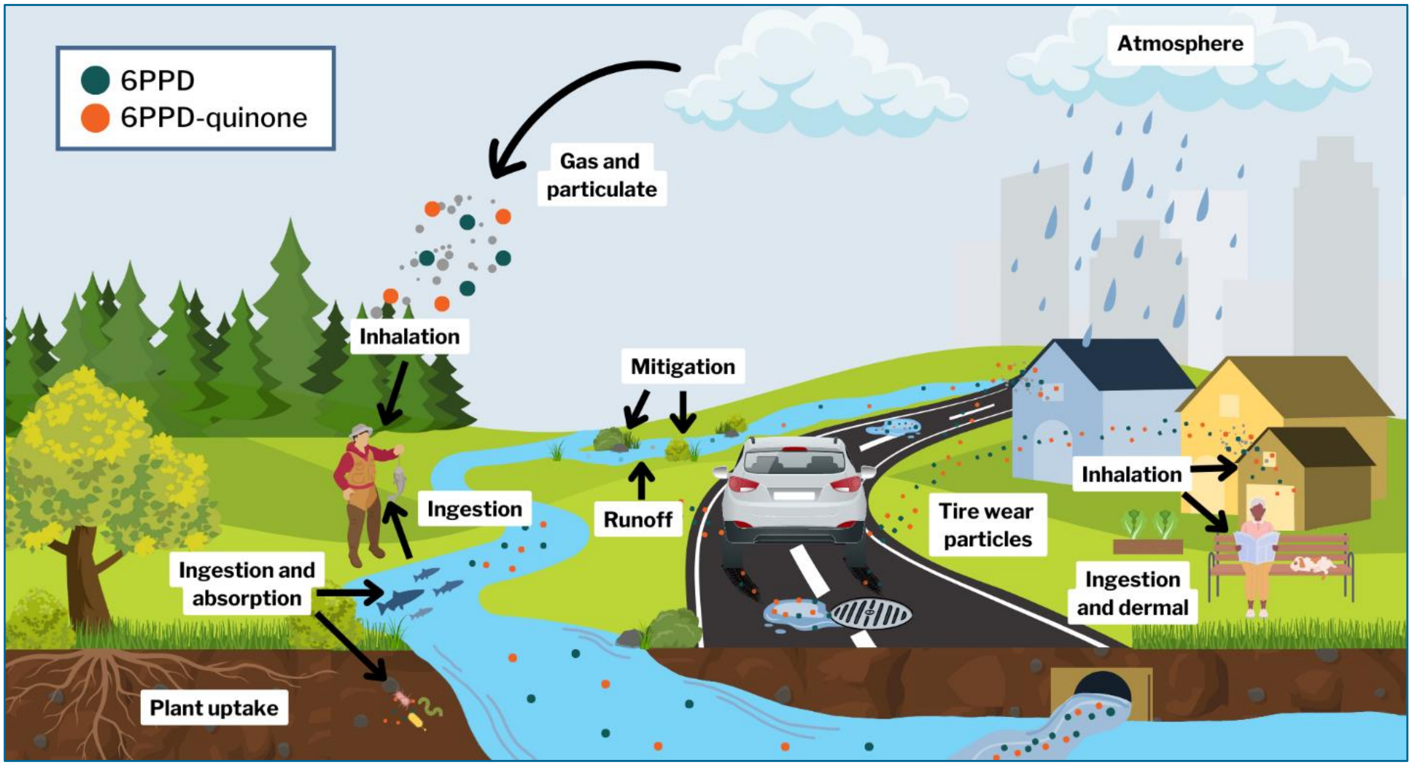


Figure 2. 6PPD in tires is converted to 6PPD-quinone (6PPD-q) when exposed to ozone. 6PPD-q is contained in tire wear particles that can be transported in the air and potentially inhaled by people. The particles can also be deposited on surfaces, soils, and plants, including foods, leading to potential plant uptake and human dermal exposure and ingestion. Tire wear particles can also stay near the roadway and be transported to surface waters through stormwater drains and runoff. 6PPD-q in surface waters can be ingested and absorbed by fishes. Exposed organisms can be ingested by humans and other species. 6PPD-q can potentially be mitigated by green stormwater infrastructure. Research is ongoing to further define 6PPD-q's environmental behaviors, exposures, and the potential development of adverse health outcomes. Figure credit: Hannah Vinyard, Washington State Department of Ecology.

Ecological Toxicity

Both 6PPD and 6PPD-q surpass the threshold for *very high* acute aquatic toxicity using the Globally Harmonised System of Classification and Labeling of Chemicals.[18] This section focuses on 6PPD-q, which ranks as one of the most potent acute aquatic toxicants when compared to chemicals with existing Clean Water Act[2] Aquatic Life Ambient Water Quality Criteria. Most of the ecological toxicity data generated thus far focuses on the acute freshwater aquatic toxicity of 6PPD-q. Two studies on the toxicity of 6PPD-q to marine organisms have been conducted,[19,20] but no studies have been done on the toxicity of 6PPD-q to the estuarine and marine stages of salmonids, which represents a significant data gap. Sublethal effects and chronic toxicity of

6PPD-q are being investigated. There is limited research regarding its toxicity to terrestrial species (e.g., *Caenorhabditis elegans*[21–23]).

Acute Toxicity. Research to date has demonstrated acute toxicity to 6PPD-q in only a few species within the salmonid family, which includes salmon, char, and trout (Table 1). Coho salmon are the most sensitive species documented, with a median LC_{50} concentration (50% mortality in lab tests) of 0.08 µg/L and death occurring within hours.[1,2,4,24] Toxicity to 6PPD-q does not follow a phylogenetic relationship. Species within the *Oncorhynchus* genus show radically different acute toxicities, from an LC_{50} as low as 0.040 µg/L in coho hatchlings[24] to no mortality observed in sockeye at 50 µg/L.[25] Some salmonids in the *Salvelinus* genus (white-spotted char[26] and brook trout[3]) are acutely sensitive at relatively low concentrations (see Table 1), while others are not.[3] *Oncorhynchus mykiss*, which encompasses rainbow trout (freshwater only) and steelhead (ocean-going), show mortality at higher doses and a slower onset of symptoms in response to 6PPD-q.[3] The LC_{50} for Chinook salmon is well above environmentally relevant concentrations[25]; however, Chinook had a low level of mortality when exposed to undiluted roadway runoff.[27] Salmonids that do not experience acute toxicity to 6PPD-q include sockeye salmon,[25] Arctic char,[3] Atlantic salmon, and brown trout,[28] as well as two varieties of Asiatic salmon: southern Dolly Varden and cherry salmon.[26]

Table 1. Reported 6PPD-quinone LC_{50} concentrations (50% observed mortality) of salmonids.

Species	LC_{50} (µg/L)	Test duration (h)	Toxicity Key
Coho salmon (*Oncorhynchus kisutch*)	0.04, [24] 0.08, [25] 0.095 [2]	24	Higher
White-spotted char (*Salvelinus leucomaenis pluvius*)	0.51 [26]	24	
Brook trout (*Salvelinus fontinalis*)	0.59 [3]	24	
Rainbow trout/steelhead (*Oncorhynchus mykiss*)	0.64,[29] 1.0,[3] 2.26 [5]	96	
Chinook salmon (*Oncorhynchus tshawytscha*)	67.3 [24], 82.1 [25]	24	
Sockeye salmon (*Oncorhynchus nerka*)	Not acutely toxic at 50 [25]	24	Lower
Atlantic salmon (*Salmo salar*)	Not acutely toxic at 12.2 [28]	48	
Brown trout (*Salmo trutta*)	Not acutely toxic at 12.2 [28]	48	
Arctic char (*Salvelinus alpinus*)	Not acutely toxic at 12.7 [3]	24	
Southern Dolly Varden (*Salvelinus curilus*)	Not acutely toxic at 3.8 [26]	48	
Cherry salmon (*Oncorhynchus masou masou*)	Not acutely toxic at 3.5 [26]	48	

Note: Example species in the table are listed from very high to low across a toxicity gradient based on the LC_{50} value, with the following ratings: coho = very high; white-spotted char and brook trout = high; rainbow trout / steelhead = medium high; Chinook salmon = medium low; and sockeye salmon, Atlantic salmon, brown trout, Arctic char, southern Dolly Varden, and cherry salmon = low. Chinook salmon were assigned medium-low toxicity out of an abundance of caution. They have an LC_{50} above environmentally relevant concentrations and potentially above some of the salmonids listed below it in the table. Nevertheless, Chinook showed low levels of mortality in undiluted roadway runoff, which could be a result of 6PPD-q or another contaminant. Until further research clarifies whether any life stage of Chinook experiences acute mortality in response to 6PPD-q at potentially environmentally relevant exposures, they were assigned medium-low toxicity.

Chum salmon (*Oncorhynchus keta*) do not show toxicity to roadway runoff[27] or tire leachate[30] but have not been tested with 6PPD-q. Outside the salmonid family, environmentally relevant concentrations of 6PPD-q (up to 2.8 µg/L) are not fatal to several fishes (white sturgeon,[3] zebrafish, and medaka[31]) and aquatic invertebrates (*Daphnia* and the crustacean (*Hyalella azteca*).[31] Toxicity studies on 6PPD-q in marine invertebrates, *Brachionus koreanus*[19] and *Parhyale hawaiensis,*[20] indicated no acute toxicity.

Acute symptoms mimic respiratory distress and include gasping at the water's surface, fin splaying, and loss of equilibrium[32]; onset of symptoms can occur within 90 minutes.[1] Examples of the effects are shown in the Puget Soundkeeper — Longfellow Creek coho salmon video. Scientists are still working to determine how 6PPD-q causes mortality in fish. Researchers have demonstrated exposure to roadway runoff causes fluid to leak out of the blood vessels in the gills and brain of coho, demonstrating that the blood–brain barrier is compromised in coho.[33] Mahoney and colleagues provide evidence that energy production at the cellular level may be disrupted.[34] The researchers further suggest that the potential inability of sensitive species to metabolize 6PPD-q into a less toxic form may contribute to its selective toxicity.[34]

Sublethal toxicity. It is still unknown whether 6PPD-q causes sublethal toxicity in wild fish populations. Sublethal effects could impact growth and reproduction and make fishes susceptible to other stressors, such as pathogens, higher temperatures, or other poor water quality parameters. Additional studies are needed to determine the concentrations of 6PPD-q that could result in adverse effects to salmonids, particularly because some populations are protected under the Endangered Species Act.

Limited work has been done studying sublethal effects in zebrafish, where 6PPD-q influenced embryo movement and heart rate.[35] In addition, environmentally relevant concentrations of 6PPD-q have been shown to alter the central nervous system of zebrafish, changing their exploratory behavior, wake/sleep cycle, and heart rate.[36] Beyond fish, chronic toxicity of 6PPD-q has been studied in *C. elegans,* a soil-dwelling round worm. The worms have neurobehavioral changes and show symptoms of oxidative stress at concentrations starting as low as 0.1 µg/L.[21,22] At 1 µg/L the worms have diminished reproductive capacity.[23] How these results translate to salmonids that are more susceptible to acute toxicity and how these sublethal effects relate to survival of aquatic species require further research.

Human Health

This section provides the most salient (e.g., not comprehensive) toxicological information on 6PPD and 6PPD-q. The health effects of 6PPD are better characterized than 6PPD-q. The health hazards of other 6PPD transformation products remain another notable data gap.[37]

6PPD. 6PPD is a well-documented skin sensitizer, resulting in allergic contact dermatitis in sensitized individuals.[38] 6PPD is also listed as a category 1B reproductive toxicant by the European Chemicals Agency (ECHA).[39] Exposed rats experienced prolonged and difficult birth, including some pregnant rats to the point of death.[39] The no adverse effect level for reproduction is 7 mg/kg body weight per day for females.[39] 6PPD increased fat accumulation in liver in mice that were given oral doses of 10 mg/kg body weight per day for 6 weeks.[40] Similarly, ECHA identified the liver and blood cells as targets of toxicity in a 28-day oral exposure rat study. Effects on the liver were reversible at 20 mg/kg body weight per day, and both sexes showed fat deposition in the liver and anemia at 100 mg/kg body weight per day.[39]

6PPD-quinone. 6PPD-q is predicted to cause oxidative stress.[41] 6PPD-q increased lipid accumulation in the livers of mice that were given oral doses of 10 mg/kg body weight per day for 6 weeks.[40] In addition, 6PPD-q increased liver triglycerides at all doses tested (10, 30, and 100 mg/kg body weight per day).[40]

Human Exposure. 6PPD and 6PPD-q were detected in human urine in a Chinese study.[17] Pregnant women's urine had the highest levels of 6PPD and 6PPD-q out of all the demographic groups in the study.[17] One predicted route of exposure to these chemicals is inhalation of particulates, with the highest potential for exposure occurring near traffic (see Figure 2). Ingestion and incidental contact with rubber products or dust may be other sources of exposure to the chemicals.[42] 6PPD and 6PPD-q are present in tire crumb rubber, and these compounds have been identified in the bioaccessible fraction after extraction of crumb rubber with simulated gastrointestinal fluid, implying they may be absorbed after ingestion.[43] The risk of 6PPD and 6PPD-q to people who consume high levels of aquatic species has yet to be characterized. There are limited studies on the bioaccumulative properties of 6PPD and 6PPD-q. Fang and colleagues suggest that 6PPD and 6PPD-q may bioaccumulate in the livers of lab mice[40]; however, additional information regarding absorption, distribution, metabolism, and excretion by the exposed mice is needed to draw this conclusion. Contaminated sources for drinking water could potentially result in exposure depending on the source water and treatment method. Research is ongoing to address this question. Johannessen and colleagues reported negative findings in treated drinking water from two Canadian facilities.[44] No test results for U.S. drinking waters have been reported.

Environmental Justice and Tribal Government Considerations

The extent of 6PPD and 6PPD-q impacts on vulnerable populations and overburdened communities will be determined as knowledge advances. Communities near roadways are disproportionally comprised lower-income people and people of color, making the potential impacts of airborne 6PPD and 6PPD-q on these communities a notable environmental justice concern.[45,46] Environmental justice considerations include but are not limited to food safety of fish consumption, drinking and recreational water safety, use of recycled rubber products, traffic proximity and air particulate matter exposure, socioeconomic impacts to subsistence and commercial fishers, and cumulative impacts.

Salmonid mortality, which can be caused by 6PPD-q, other toxic chemicals, climate change, habitat loss, and additional factors,[18] disproportionately impacts tribal nations in North America by threatening tribal treaty rights, access to traditional foods, and the cultural and economic well-being of Indigenous peoples. Fishing rights for many tribal nations are guaranteed by treaties that have been signed, ratified, and reaffirmed by the U.S. government. Concerns for tribal nations around 6PPD-q include impaired salmon recovery and hatchery efforts, sublethal impacts to fishes, reduced ecosystem resilience, and cumulative impacts to fishes and peoples.

Fate and Transport

Stormwater is the primary transport mechanism for 6PPD-q to surface water. TWPs are generated as tires roll across the road, particularly during acceleration, braking, and turning. These particles, and the chemicals they contain, collect in road dust until stormwater transports them into the aquatic environment. In many cities in the United States, stormwater is diverted to wastewater treatment plants (WWTPs) through combined sewer and stormwater systems. Studies investigating 6PPD-q removal in WWTPs' have had mixed results. Several studies showed a strong reduction or removal of 6PPD-q to nondetect levels,[10,47,48] and another study showed an increase in mass in the effluent from the WWTP.[49] More research is needed to follow up on this. The presence of 6PPD and 6PPD-q in biosolids from WWTP remains a data gap.

The levels of 6PPD-q are highest during or following rain or snowmelt runoff[8,47] and have been measured in U.S. surface waters at concentrations above the LC_{50} values (see Table 1) for coho, brook trout, and potentially rainbow trout.[1,2] The levels of 6PPD-q in the water column can stay elevated for days[6,8]; the duration depends on the frequency of inputs, the site, and the characteristics of the receiving water. Fate and transport of the chemicals in estuaries and saltwater has not yet been characterized. 6PPD-q is expected to sorb to sediment or particles[18,50] and has been measured in sediment in China.[15] Additionally, TWPs may be airborne initially and could be transported long distances. The chemical and physical properties of 6PPD-q in the atmosphere are currently unknown. Notably, 6PPD-q has been measured in particulate matter, including in airborne particles less than 2.5 µm ($PM_{2.5}$),[14,51,52] road dust,[12,53] and household dust.[12] The highest detections and concentration ranges measured in various environmental media are provided in Table 2).Table 2Table 2. 6PPD-quinone concentrations measured in roadway runoff, surface water, sediment, and particulate matter-2.5.

Media	Concentration Range	Notes	References
Roadway runoff	ND – 2.43 µg/L	Highest detection was in China by Cao et al.	2,6,9,10,54
Surface water	ND – 2.8 µg/L*	Highest detection was in the Don River in Toronto, Canada, roughly 35× higher than median coho LC_{50}. Loading generally correlates with the amount of rainfall.	2,7,8,54–56
Sediment	ND – 18.2 ng/g	Highest in urban river sediment, present in deep sea sediment in China.	15
Particulate matter (up to $PM_{2.5}$)	0.1 – 7,250 pg/m^3	Highest detection alongside a road in Guangzhou, China.	14,51,52

*Median LC_{50} for coho (0.08 µg/L), brook trout (0.59 µg/L), and rainbow trout (1.0 µg/L) (see Table 1).

Notes: µg/L = microgram per liter, ng/g = nanogram per gram dry weight, ND = nondetect, pg/m^3 = picogram per cubic meter

Monitoring and Analytical Methods

Monitoring for 6PPD and 6PPD-q in air, soil, surfaces, and water is challenging because environmentally relevant concentrations may be low and presence may be intermittent. Sampling studies indicate that 6PPD-q is detected at higher concentrations during or following rain and snowmelt events that occur following an extended dry period.[8,56] The rate of transport of stormwater and exposure to aquatic life increase with percent impervious surface within a watershed.[8,56] Studies have shown that 6PPD-q can persist for days in urban areas during or following storm events.[8,57] Efforts are underway by the state of Washington to evaluate passive sampling technologies and effectiveness.

The U.S. Environmental Protection Agency is developing a 6PPD-q test method for surface water and stormwater that is projected to be available late in 2023. *Standard Operating Procedure (SOP): Extraction and Analysis of 6PPD-q* (Mel730136, Version 1.2)[58] contains procedures for the extraction and the qualitative and quantitative analysis of 6PPD-q by triple quadrupole mass spectrometry. The standard operating procedure recommends the sample collection, preservation, storage, and holding times. In addition, several commercial and research laboratories can test for 6PPD-q in water.

Other media. Standardized methods are currently in development for sediment and biological tissues. 6PPD-q has been measured in the air by academic researchers,[14,51,52] but there is not a verified method for regulatory testing.

Stormwater Best Management Practices

Stormwater research is focused on determining the effectiveness of existing and new BMPs at 6PPD-q removal, modifying stormwater systems to improve 6PPD-q removal, adding BMP retrofits to urban roadways that lack adequate space for green infrastructure, and refining green stormwater infrastructure to maximize 6PPD-q filtration.

Effective Stormwater Mitigation Technologies. A recent Washington State publication[59] evaluated stormwater BMP treatment mechanisms and rated their expected 6PPD and 6PPD-q removal effectiveness. Several source control, flow control, and runoff treatment stormwater control measures were found to be potentially effective solutions. Washington State is funding research to verify the efficacy of these BMPs and stormwater control measures.

Researchers have demonstrated that running stormwater through the bioretention soil mix (stormwater compost and sand) that is designed as a component of a bioretention system (Figure 3) prevents acute mortality in coho.[60,61] Research to optimize the depth and composition of the bioretention soil mix to maximize the effectiveness and longevity of the system is ongoing. Additionally, different media are being tested to reduce potential nutrient leaching from bioretention BMPs. Preliminary results of a study representing an accelerated timeline of 10 water years by passing water contaminated with 6PPD-q through a laboratory-managed bioretention soil mix shows prevention of coho mortality over the 18-month study period; the results of this study are being prepared by McIntyre and colleagues.

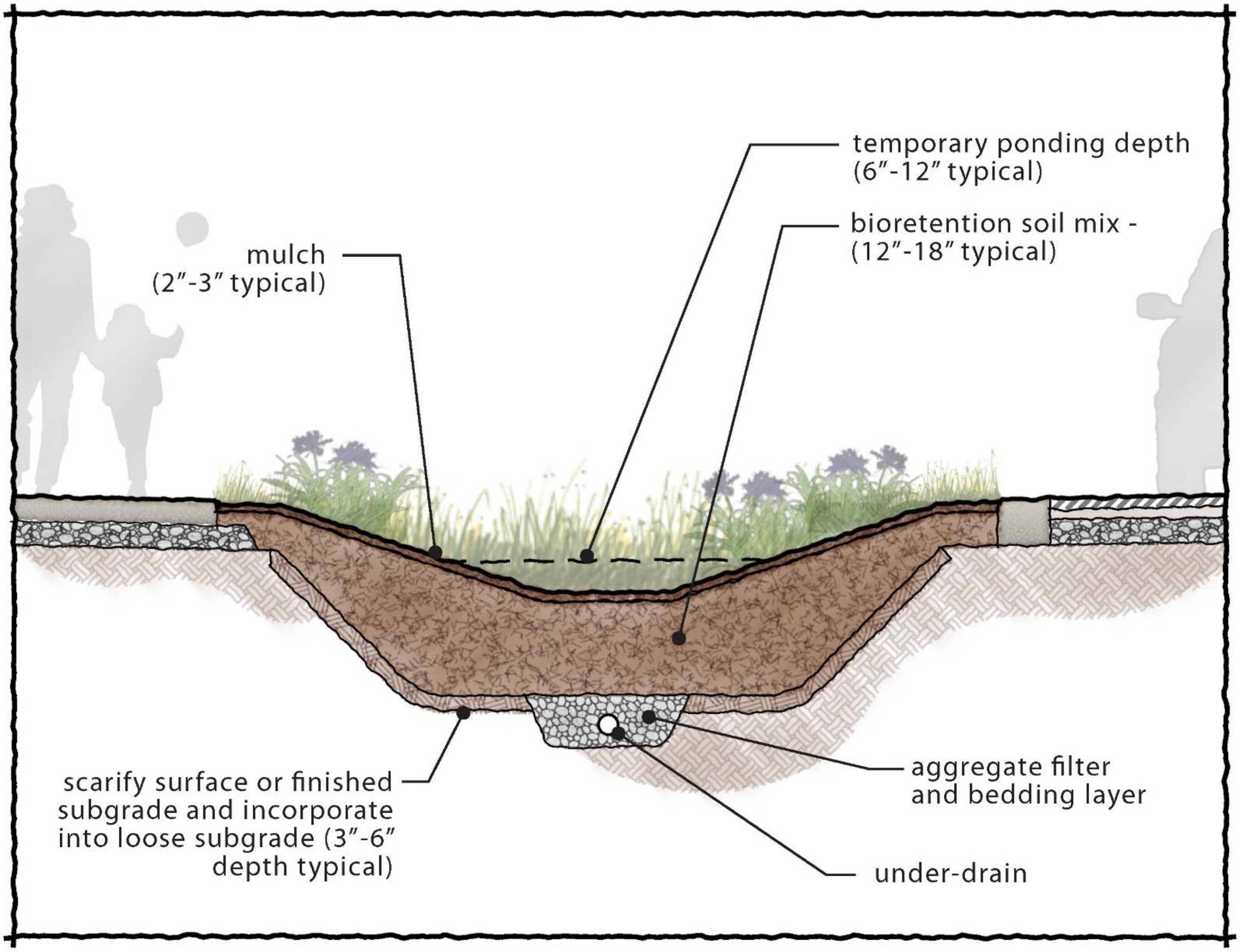


Figure 3. Typical bioretention system with design features. Current research is focused on optimizing the depth and composition of the bioretention soil mix. Courtesy of AHBL, Inc.

Researchers are also using compost-amended biofiltration swales comprising topsoil, compost, and vegetation (Figure 4) to determine the effectiveness of biofiltration systems alongside roadways; the results of this study are being prepared by Tian and colleagues. Preliminary results of the study show variability in compost-amended biofiltration swales performance across seasonal and storm specific parameters, with an efficiency of up to 80+% removal of 6PPD-q.

Identifying Vulnerable Aquatic Areas.
Washington State is developing strategies to focus sampling and stormwater mitigation efforts in locations where 6PPD-q is having a critical environmental impact. The development of these strategies is based on collaboration with tribal governments, community engagement, and available GIS mapping tools containing parameters that are assumed to influence concentrations of 6PPD-q in surface waters.

Figure 4. Example of a compost-amended biofiltration swale. Stormwater is filtered as it flows along the grass in the swale and infiltrates into the topsoil and compost. Photo: Washington State Department of Transportation.

Factors used to identify these areas include, but are not limited to, level of traffic, impervious surfaces, precipitation, media composition that stormwater travels through to get to receiving water, size of the receiving water, and the presence of sensitive species.

Other ongoing research includes the effectiveness of permeable pavement to capture tire particles, analysis of different compost medias and biochar to determine the effectiveness of organic matter in bioretention systems, and evaluation of existing street-sweeping technologies and practices (timing and frequency) on removal of 6PPD and 6PPD-q from roadways.

Alternatives to the Use of 6PPD in Tires

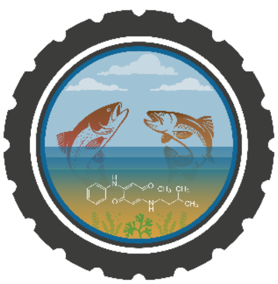
Identifying and deploying alternatives to 6PPD in tires can ultimately reduce or eliminate 6PPD-q in the environment. Currently, 6PPD is necessary for tire safety and to extend the life of tires by preventing cracking and degradation caused by ozone. Discussions with tire manufacturers have revealed that an anti-degradant is not currently available to replace 6PPD. Tires are complex products with tire safety as a principal design priority, and a fully functional anti-degradant is a necessity. Research is ongoing to identify safer alternative chemicals that provide the functionality of 6PPD in tires.[62] Due to the complexity of identifying, testing, and implementing a suitable alternative to 6PPD, the U.S. Tire Manufacturers Association cannot estimate the time frame for the replacement at this stage of the process. The states of California and Washington are pursuing policies to promote the advancement of alternatives to 6PPD in tires.

State Policies and Regulations

Washington State is developing a statewide action plan, funding research to fill in data gaps, assessing other potential tire anti-degradants, and developing specific data requirements and standards to assess the hazards of the alternatives. Technical Memo: Assessment of Potential Hazards of 6PPD and Alternatives[63] provides an overview of known toxicological hazards of chemicals that are or have been used as anti-degradants in tires. Washington State is currently developing hazard criteria to define “safer” when looking at alternatives to 6PPD. There is currently no estimated timeline for completion of the action plan or alternatives assessment. The Safer Products for Washington program, which aims to reduce toxic chemicals in consumer products, identified 6PPD as a priority chemical. Washington and California supported the Collaborative Innovation Forum: Functional substitutes to 6PPD in tires to develop a road map for identifying safer alternatives to 6PPD.[62]

California's Department of Toxic Substances Control will begin regulating 6PPD in motor vehicles through the Safer Consumer Products Program on October 1, 2023. These regulations require tire manufacturers to analyze the hazards and adverse environmental impacts of potential alternatives to 6PPD, as well as evaluate the benefits and tradeoffs of replacing 6PPD. This process leverages the technical expertise of the tire manufacturers and enables them to meet vehicle safety and consumer product safety requirements, while providing a rigorous, transparent, and scientific framework to evaluate and compare potential alternatives to 6PPD. The tire manufacturers' initial screening of potential alternatives is due on March 29, 2024.

6PPD is on Minnesota's Toxic Free Kids Act Chemicals of High Concern List,[64] and the state's legislature appropriated nearly half a million dollars for research on 6PPD-q and its effect on state fishes.[65] Maine also includes 6PPD on its Chemicals of Concern list.[66]



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This fact sheet incorporates data through July 2023.

The **Interstate Technology and Regulatory Council** (ITRC) is a state-led environmental coalition working to create innovative solutions and best management practices. ITRC produces documents and training that broaden and deepen technical knowledge and expedite quality regulatory decision-making while protecting human health and the environment. In January 2023, ITRC started the Tire Anti-degradants (6PPD) Team to provide guidance documents and tools on 6PPD and 6PPD-quinone for environmental officials.

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